REMARKS

No new matter has been added in the amendments to the claims. Claims 1-7 have been canceled solely as directed to the non-elected invention. In addition, Claim 8 has been amended solely to introduce the definition of the term "purified botulinum toxin" contained within the specification at page 5, lines 16-24. As defined therein, the purified botulinum neurotoxin is a neurotoxin which is separated from a non-toxic protein constituting a botulinum toxin (progenitor toxin). While the progenitor toxin is a purified botulinum toxin complex having a molecular weight of from about 300 KD to 500 KD, the separated neurotoxin usually has a molecular weight of 150 KD. In the present invention, only the neurotoxin among the constituents of the progenitor toxin is used. Thus, the amendment to the claim simply makes explicit the definition of the term that was already recited in the claim. As such, the amendment has been made for reasons unrelated to patentability.

Finally, Claims 10-16 have been added to more specifically claim the Applicants' invention. Applicant notes that in the restriction requirement mailed October 31, 2005, that the Examiner had required an election of species between the types of botulinum toxin recited in Claim 4 if Group I had been elected. Since Group III was elected, no election of species was made in response to the restriction requirement. Nevertheless, Claim 12 has now been added containing a limitation similar to that formerly recited in Claim 4. To the extent that the Examiner now requires an election of species with regard to the elected invention, Applicants elect botulinum toxin type A.

Anticipation Rejection

Claims 8 and 9 have been rejected under 35 U.S.C. 102(b) as being anticipated by Johnson et al. (US 5,696,077). Johnson et al. ('077) disclose a method of treating muscle hyperactivity, comprising administering a purified botulinum toxin to a patient with muscle hyperactivity. The purified botulinum toxin is *C. botulinum* type B neurotoxin complexed with botulinum-derived stabilizing proteins (col. 10, lines 52-65 and col. 12, lines 11-16). That is, the purified botulinum toxin referred to in Johnson et al. ('077) is the progenitor toxin specifically excluded from Claim 8, i.e. a botulinum toxin complex of about 300 to about 500 KD. The progenitor toxin is the same as BOTOX which is used as a control in the Example 3. The purified

botulinum neurotoxin (150 KD neurotoxin) recited in the claims is, therefore, distinguishable from the purified botulinum toxin referred to in Johnson et al. ('077).

Johnson et al. ('077) describe that the toxin and associated non-toxic binding proteins of the complex were separated (col. 7, lines 15-17). However, Johnson et al. ('077) are quite silent about the use of the separated toxin for treating muscle hyperactivity. The Examiner has stated that the muscle hyperactivity diseases resulting from various diseases involving involuntary muscle movements and spasms require a fast-acting remedy, as these are painful and debilitating conditions. However, Johnson et al. ('077) suggest nothing about the advantage obtained by the use of the purified botulinum neurotoxin (150 KD neurotoxin) compared with the use of the progenitor toxin such as that sold under the tradename BOTOX. The advantage of the use of the present invention compared with the use of the progenitor toxin is clearly evidenced by Examples 3, 4 and 6 in the present specification. The present invention exhibits far faster treatment effects than the progenitor toxin. Thus, the present invention is particularly advantageous when used in the treatment of a disease that needs treatment with a fast acting remedy.

In view of the foregoing, the rejection should be reconsidered and withdrawn.

Rejection over Borodic in view of Johnson et al. ('070)

Claims 8 and 9 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Borodic (US 5,183,462) in view of Johnson et al. (US 5,939,070). Borodic discloses a method of treating muscle hyperactivity, comprising administering a partially purified botulinum toxin to a patient with muscle hyperactivity. As the Examiner has admitted, Borodic does not disclose that the toxin in the pharmaceutical preparation is in the fully purified form. The disclosed example of the botulinum toxin is OCULINUM available from Allergan Pharmaceuticals, Inc. which is a progenitor toxin. Borodic is quite silent about the use of the purified 150 KD neurotoxin.

Johnson et al. ('070) disclose a hybrid botulinal neurotoxin comprising heavy and light chain combinations that are not present in nature. Johnson et al. ('070) also disclose a method for creating the hybrid neurotoxin by isolating botulinal neurotoxin heavy and light chains from the botulimum toxin and linking the heavy and light chains into a hybrid neurotoxin with a linker. The heavy and light chains are not of the same serotype. Johnson et al. ('070) suggest that this hybrid toxin molecule is used to avoid the immune response of the patient (col. 6, lines 1-10). As is seen from the fact that no animal model experiment is conducted in Johnson et al., Johnson et

al. ('070) are quite silent about the use of the 150 KD neurotoxin for treatment of the muscle hyperactivity and the treatment effect thereof. Thus, the concept of the Johnson et al. ('070) is different from that of the present invention.

Thus, even if the cited references are combined, the use of the 150 KD neurotoxin for treatment of the muscle hyperactivity is not described. Thus, no *prima facie* showing of obviousness can be established by the cited references. Moreover, even if there were a *prima facie* showing of obviousness, the unexpected advantage of the present invention would clearly evidence its nonobviousness. That is that the use of the 150 KD neurotoxin unexpectedly provides a treatment effect much more rapidly than the toxins of the prior art. This advantage is particularly important when used on a patient that needs treatment with a fast-acting remedy. These advantages would not be expected from either of the cited references. Accordingly, the rejection should be reconsidered and withdrawn.

Rejection over Donovan in view of Johnson et al. ('070)

Claims 8 and 9 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Donovan (US 2001/0053369) in view of Johnson et al. (US 5,939,070). Like the Borodic reference described above, Donovan discloses a method of treating muscle hyperactivity, comprising administering a partially purified botulinum toxin to a patient with muscle hyperactivity. As the Examiner has admitted, Donovan does not disclose that the toxin in the pharmaceutical preparation is in the fully purified form. Donovan is quite silent about the use of the 150 KD neurotoxin and the advantage thereof.

Johnson et al. ('070) is the same reference discussed above in connection with the rejection in which it is combined with Borodic. Even if this reference were combined with Donovan, the use of the 150 KD neurotoxin for treatment of the muscle hyperactivity and its advantage that a treatment effect on a patient of the muscle hyperactivity that needs treatment with a fast-acting remedy is exhibited faster than the progenitor toxin, are not expected from the combination. Accordingly, this rejection should also be reconsidered and withdrawn.

Rejection over Aoki et al. in view of Johnson et al. ('070) and Allergan, Inc.

Claims 8 and 9 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Aoki et al. (US 6,319,505) in view of Johnson et al. (US 5,939,070) and Allergan, Inc. (package

insert for Botox®). Aoki et al. disclose a method of treating muscle hyperactivity, comprising administering a partially purified botulinum toxin to a patient with muscle hyperactivity. As the Examiner has admitted, Aoki et al. do not disclose that the toxin in the pharmaceutical preparation is in the fully purified form. Aoki et al. are quite silent about the use of the 150 KD neurotoxin and the advantage thereof. Johnson et al. ('070) is discussed above, while Allergan, Inc. simply discloses that Botox is a purified neurotoxin complex. None of these references suggest the use of the 150 KD neurotoxin as presently claimed.

Even if the cited references are combined, therefore, the use of the 150 KD neurotoxin for treatment of the muscle hyperactivity and its advantage that a treatment effect on a patient of the muscle hyperactivity that needs treatment with a fast-acting remedy is exhibited faster than the progenitor toxin, are not expected from the combination. The rejection should be reconsidered and withdrawn.

Rejection over Graham in view of Johnson et al. ('070), Allergan, Inc., and Shore Laser

Claims 8 and 9 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Graham (US 6,395,277} view of Johnson et al. (US 5,939,070), Allergan, Inc. (package insert for Botox@) and Shore Lasor("Botulinum toxin for the treatment of facial lines and wrinkles") .

Graham discloses a method of treating muscle hyperactivity, comprising administering a partially purified botulinum toxin to a patient with muscle hyperactivity. As the Examiner has admitted, Graham does not disclose that the toxin in the pharmaceutical preparation is in the fully purified form. Graham is quite silent about the use of the 150 KD neurotoxin and the advantages thereof.

Johnson et al. ('070) and Allergan, Inc. are discussed above. Shore Laser simply discloses that Oculinum is an earlier name for Botox. Even if the cited references are combined, therefore, the use of the 150 KD neurotoxin for treatment of the muscle hyperactivity and its advantage that a treatment effect on a patient of the muscle hyperactivity that needs treatment with a fast-acting remedy is exhibited faster than the progenitor toxin, are not expected from the combination. The rejection should be reconsidered and withdrawn

Conclusion

In view of the foregoing, the application is presented as fully in condition for allowance. Should there be any questions concerning this application, the Examiner is invited to contact the undersigned attorney at the telephone number appearing below. Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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